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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/707,167	11/07/2000	Maurice Maloney	9369-161	8170

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EXAMINER	
LIU, SAMUEL W	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/707,167	MALONEY ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,20 and 22-35* is/are pending in the application.

4a) Of the above claim(s) *none* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,20 and 22-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 18, 20 and 22-35 are pending.

Applicants' amendment filed 7 November 2003, which amends claims 22, 25 and 33 has been entered. Also, applicant's request (filed 7 November 2003) for extension of time of two months has been entered. Note that applicants' amendment filed 6 March 2003 cancels claims 19 and 21 and adds claims 34-35, and applicants' preliminary amendment filed 6 March 2002 cancels claims 1-17 and adds claims 29-33.

The following Office Action is applicable to the pending claims 18, 20 and 22-35.

Please note that grounds of objection and/or rejection not explicitly restated and/or set forth below are withdrawn.

Terminal Disclaimer

The terminal disclaimer filed on 6 December 2003 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of US Application No. 10/260960 and date of US Pat. No. 6509453 has been reviewed and is accepted.

Objection to the specification

The disclosure is objected to because of the following informalities:

The specification defines the "target molecule" as the molecule that one wants to purify, which can be recombinantly produced or obtained from natural source (see page 10). Yet, the specification also sets forth that the target molecule includes protein that binds directly to oil bodies (see page 4). It appears ambiguous that target molecule does or does not encompass oil-

body proteins (i.e., proteins naturally bound to oil bodies) including oleosin, for example. Clarification in this regard is required.

The followings are the new groudnd of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18, 20 and 22-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites "associates with the oil bodies"; the recitation is unclear as to whether or not "associates with" refers to that interact with oil bodies via a direct (*covalently or non-covalently*), or via an indirect mean. See also claims 22 and 29. Additionally, claim 18 (item 1) is unclear in " the target molecule" because the claim does not make it clear as to whether or not said target molecule refers to a recombinant polypeptide to be isolated or an oil-body protein. See also claim 29. Further, claim 18 appears to be missing a step which refers to how the oil bodies are accessible to target molecule or/and the recombinant polypeptide in order to allow the oil bodies to contact with the target molecule and a ligand protein (see claim 18, item 1). Please note that claim 18 is directed to a method of isolating a recombinant polypeptide from a cell; thus, the claim must clarify how to make contacting the oil bodies with the ligand and the recombinant polypeptide. The dependent claims are also rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 18, 22-23 and 26-28 are rejected under 35 U.S.C. 102 (b) as being anticipated by Moloney, M. (WO 9621029).

Moloney teaches expression of oleosin/collagenase fusion protein in *B, napus* cells (see page 50). Thus, Moloney teaches a method of isolating a polypeptide (a recombinant polypeptide) comprising contacting oil bodies with a protein ligand (i.e., oleosin) that associates with the oil bodies and said polypeptide, and isolating said oil bodies associated with said polypeptide that is to be isolated. The Moloney teaching is applied to the instant claim 18.

Moloney teaches a method of isolating a recombinant protein (e.g., enzyme) from a cells

(e.g., enzyme) comprising (i) introducing into the cell a polynucleotide encoding the said recombinant protein and a protein ligand (e.g., oil-body protein [OBP]) which is recombinantly fused to said recombinant protein; (ii) growing the cell (see the patent claims 1 and 12), and (iii) isolating said protein from the cell sample (see the patent claims 12, and page 2). The Moloney's teaching is applied to the application claim 22. It should be noted that (**A**) claim 22 as written does not exclude possibility that the recited first and second polynucleotides are in a fusion construct, i.e., the polynucleotides encode a fusion polypeptide between the protein ligand and the recombinant protein; (**B**) the specification defines ligand as a molecule that can associates with both the target (recombinant) molecule and oil bodies (see page 10, the last paragraph); thus, according to this definition, OBP can act as a ligand. (**C**) here, said ligand meets the limitation that the ligand is capable of associating with said recombinant protein and said oil bodies; and (**D**) claim 22 as written does not exclude that said ligand is a protein which naturally binds with oil bodies. Therefore, Moloney anticipates the application claim 22.

Since the above said the ligand (OBP) is recombinantly fused with the protein of interested, the ligand therefore is not naturally associated with oil bodies, which meets the limitation set forth in the instant claim 23.

Also, Moloney teaches a composition comprising oil bodies associated with a ligand (oleosin) that covalently linked (fused) to a target protein (an enzyme) (see page 3, lines 1-3), which anticipates claims 26-28 of the instant application. Please note that claims 26 and 27 do not limit that the ligand is NOT oil-body protein, i.e., oleosin, and the specification has defined ligand as a molecule that can associates with both the target (recombinant) molecule and oil

bodies (see page 10, the last paragraph). Thus, the Moloney's teaching is applicable to claims 26-28.

Because here the oleosin protein is not a naturally occurring but rather recombinantly generated in a fusion protein from, the instant claim 28 is anticipated by the above stated Moloney's teaching.

Claims 18, 20, 22-28 and 29-30, 32 and 34-35 are rejected under 35 U.S.C. 102 (b) as being anticipated by Moloney, M. (WO 9321320).

Moloney teaches a method of isolating a recombinant protein (e.g., enzyme) comprising (i) contacting oil bodies (OB) with a protein ligand (an antibody) that associated with the OB through binding to an oil-body protein (OBP) and contacting with the recombinant protein, and (ii) isolating said the recombinant protein that associates with the OB via affinity chromatography (see abstract and page 21, the 2nd paragraph). The Moloney's teaching anticipates the application claims 18 and 20.

Since the recombinant protein (polypeptide of interest) is in a cell sample, the above teaching is applied to claims 29-30, 32 and 35 of the current application.

Moloney teaches that in the above method involve disrupting cell to allow association of OB with the recombinant protein (see the patent claims 23-25), as applied to claim 34 of the current application.

Also, Moloney teaches a method of isolating a target protein (e.g., enzyme) from a host plant cell comprising (i) introducing into the cell a polynucleotide encoding the said recombinant protein and a protein ligand (e.g., oil-body protein [OBP]) which results in fusion between the

target protein and OBP (see the patent claim 28); (ii) growing the cell, and (iii) purifying said protein from the cell sample (see the patent claim 28). The Moloney's teaching meets the limitation of the application claim 22. It should be noted that (**A**) claim 22 as written does not exclude possibility that the recited first and second polynucleotides are in a fusion construct, i.e., the polynucleotides encode a fusion polypeptide between the protein ligand and the target protein; (**B**) the specification defines ligand as a molecule that can associates with both the target (recombinant) molecule and oil bodies (see page 10, the last paragraph); thus, according to this definition, OBP can act as a ligand. (**C**) here, said ligand meets the limitation that the ligand is capable of associating with said the target protein and said oil bodies; and (**D**) claim 22 as written does not exclude that said ligand is a protein (i.e., OBP) which naturally binds with oil bodies. Therefore, Moloney anticipates the application claim 22.

Since the above-mentioned ligand is an antibody, which is not naturally associated oil bodies, the Moloney's patent anticipates the instant claim 23-24.

Moloney teaches that in order to obtain the oil bodies fraction containing OBP-recombinant polypeptide fusion, the said plant cells transferred with the polynucleotide encoding said fusion protein are disrupted by lysis of the cells (see the patent claim 31), as applied to the instant claim 25.

Also, Moloney teaches a composition comprising oil bodies associated with a ligand (oil-body protein (OBP)) that covalently linked (fused) to a target protein (an enzyme) (see page 3, lines 1-3), which anticipates claims 26-27 of the instant application. Please note that claims 26 and 27 do not exclude that the ligand is not OBP, and that the specification defines ligand as a

molecule that associates with both the target (recombinant) molecule and oil bodies (see page 10, the last paragraph). Thus, the Moloney's teaching is applicable to claims 26-27.

Because here the oleosin protein is not a naturally occurring but rather recombinantly generated in a fusion protein from, the instant claim 28 is also anticipated.

Claims 18, 20, 22-23, 25-29 and 32-35 are rejected under 35 U.S.C. 102 (a) or (e) as being anticipated by Moloney, M. (US Pat. No. 5650554).

In example 8, Moloney teaches the expression of oleosin/hirudin fusion protein in the seeds of transgenic *Brassica napus*. Thus, Moloney teaches a method for isolating a polypeptide comprising contacting oil bodies (OB) with hirudin ligand fused to the oleosin target molecule which associates with the OB through hirudin ligand, and isolating the OB associated fusion protein. The Moloney's teaching anticipates the application claim 18.

While Moloney does not teach that the antibody was recombinantly produced, this is different in recombinantly produced and naturally occurring.

Claim 20 is included in this rejection because the hirudin can be considered to be a receptor polypeptide, and the antibody acts as a ligand since it "associates" with the OB and the oleosin target molecule.

In example 3, Moloney teaches a DNA construct comprising nucleotide sequence encoding an oleosin-β-glucuronidase (GUS) fusion polypeptide. In example 4, this DNA construct was used to produce transgenic *Brassica napus*. The seeds of the transgenic *Brassica napus* showed that GUS activity specifically associated with oil bodies (OB) fraction. This illustrates that the expression and targeting of a bacterial derived enzyme specific to the OB

fraction of transgenic plants. Thus, Moloney teaches a method of separating a recombinant polypeptide by introducing a nucleotide sequence encoding oleosin and a nucleotide sequence encoding a ligand (GUS) into *Brassica napu,* and expressing these nucleotide sequences. The seeds of transgenic *Brassica napus* showed that GUS activity specifically associated with the OB fraction. Moloney teaches purifying OB fraction containing oleosin-GUS fusion protein (see column 27, lines 47-55). Because the above-mentioned oleosin protein is expressed as a recombinant polypeptide (a fusion protein) and the ligand is said GUS enzyme, the above Moloney's teaching meets the limitation set froth in the application claims 22-23.

Moloney teaches that in order to obtained the OB fraction containing the oleosin-GUS fusion protein, the seeds are disrupted, i.e., ground in an extraction buffer, as applied to claim 25 of the current application.

Since the above mentioned OB fraction is a composition comprising OB associate with GUS ligand that is covalently attached to the *target molecule*, i.e., *oleosin protein*, the above Moloney' teaching anticipates the application claims 26-28.

Moloney teaches a method for separating a target molecule (oleosin) from a sample by contacting OB with a protein ligand (GUS) and a target molecule (oleosin), and separating the OB and the target molecule from the sample (the OB fraction comprising the target molecule oleosin protein), as applied to the application claims 29 and 35.

Moloney teaches that the sample is a seed, which meets the limitation "the sample is a cell" set forth in the application claim 32.

Moloney teaches the target molecule oleosin is a protein, and GUS and oleosin were produced as a fusion polypeptide, as applied to the application claim 33.

Moloney teaches disrupting cell integrity by grounding transgenic *Brassica napu* seeds. Note that said seeds contain the OB with which GUS-oleosin associated. The Moloney's teaching thus anticipates the application claim 35.

Provisional Rejection - Obviousness Type Double Patenting

Claims 18, 20, 29-30, 32 and 34-35 of this application conflicts with claims 15, 9-10 and 15-16 of Application No. 10260562. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this

application. See 37 CFR 1.130 (b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 18, 20, 29-30, 32, and 34-35 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-5, 9-10 and 15-16 of Application No.10260562. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-5 and 10 of 10260562 sets forth a method of isolating a target (recombinant) molecule from a cell sample comprising (i) contacting oil bodies with a protein ligand fused to an oil-body protein (claim 4) and the target molecule in the sample; and (ii) separating the form target molecule associated oil bodies from said sample (claim 1). Since said ligand is not normally associated with oil bodied, and since said ligand associates with the oil bodies and said target molecule, *e.g.*, thrombin (see claim 2-5 and 10), 10260562 claims 1-5 are obvious variation of claim 18 and 29 of the current application.

Claim 16 of 10260562 sets forth that the ligand is an antibody, which is a common subject matter of claims 20 and 30 of the current application.

Claim 15 of 10260562 teaches that the sample is a cellular sample (see [0139] and [0142]); thus, the 10260562 claims 1-5 are obvious variation of claim 32 of the current application.

Since 10260562 teach that the cell (e.g., transgenic plant cell) from which the target molecule is isolated is subject to homogenization (see [0096]), i.e., disrupting cell's integrity, 10260562 claim 15 is an obvious variation of claim 34 of the current application.

Claim 9 of 10260562 sets forth that the target molecule is protein, which is the subject matter of the instant claim 35.

Therefore, the instant application and Application 10260562 claims are obvious variation, and they are not patentably distinct from each other.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22-24 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moloney, M. (US Pat. No. 5650554).

The teaching of Moloney is set forth above. Moloney does not specifically teach via example an oleosin/antibody fusion protein. However, at columns 16-17, Moloney suggests that protein or polypeptide having therapeutic or diagnostic value such as antibodies, and specifically a single chain antibody can be used as part of an oleosin fusion protein, as applied to claims 22-24 and 29-31.

I would have been obvious to one of ordinary skill in the art at the time the invention was made to separate target molecule, e.g., oleosin by contacting oil bodies with antibody (including single chain antibodies) wherein the antibody acts as a ligand because Moloney suggests oil bodies associate with oleosin/antibody fusion protein have therapeutic or diagnostic value. Since Moloney exemplifies at least two oleosin fusion proteins (GUS and hirudin, see the above

statement), it has been predictable that such the oleosin/antibody fusion protein can be recombinantly produced and associated with oil bodies.

The skilled artisan thus would have successfully arrived at the current invention regarding isolation of the antibody/oleosin fusion protein associated oil-bodies from a biological sample. Therefore, the claimed invention was *prima facie* obvious to make and use the invention at the time it was made.

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

SWL

Samuel Wei Liu, Ph.D.

March 9, 2004